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| 09/831,635 | 07/20/2001 | Joseph R. Lakowicz | 2542-139 | 6945 |

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| ART UNIT | PAPER NUMBER |
|---|---|
| 1641 | |

DATE MAILED: 05/19/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/831,635 | LAKOWICZ ET AL. | |
| | Examiner | Art Unit | |
| | Gailene R. Gabel | 1641 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *29 January 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-14* is/are pending in the application.

4a) Of the above claim(s) *13 and 14* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-12* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *7/20/01*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

### *Election/Restrictions*

1. Applicant's election of Group 1, claims 1-12, filed 1/29/04 is acknowledged and has been entered. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). Claims 13 and 14 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being claims drawn to a non-elected invention. Currently, claims 1-14 are pending, claims 1-12 are under examination.

### *Claim Rejections - 35 USC § 112*

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 1-12 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1, step c) is indefinite in reciting "capable of changing" because it fails to recite a positive limitation in the claim.

Claim 1, step e) is vague and indefinite because it is unclear how the presence and the concentration of analyte in the sample are differentially obtained, based on the correlation step. It appears that a change will provide a presence of the analyte,

whereas a degree of change is perhaps required to obtain a quantitation of the analyte concentration, such as for example by comparing results obtained with standards having known values.

Claim 6 is vague and indefinite in reciting, "stretched polymer film" because it is unclear, as recited, what is encompassed by the term "stretched" as used in the context of the claim.

Claim 8 is confusing in reciting, "wherein the method determines pH" because claim 1 from which it depends, recites a method of determining the presence or concentration of analyte by correlating a change in anisotropy between two measurements; thus, it is unclear what functional cooperative relationship exists between the pH determined in the instant claim and the analyte determined by anisotropic change recited in claim 1.

Claim 10 is vague and indefinite in reciting, "stretched film" because it is unclear, as recited, what is encompassed by the term "stretched" as used in the context of the claim.

Claim 11 is vague and indefinite in reciting, " the reference and sensing molecules are distinct molecules having the same structure" because the term "distinct" is a subjective term that lacks a comparative basis for defining its metes and bounds. Thus, it is unclear how the molecules are distinct yet have a same structure. Please clarify.

Claim 12 is indefinite in reciting "[not] capable of changing" because it fails to recite a positive limitation in the claim.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

In the art, anisotropy is a parameter that is interrelated to fluorescence polarization; both are said to describe the same phenomena. Fluorescence polarization immunoassays are based on polarization or anisotropy of emitted light when a sample is excited with vertically polarized light. Hence, anisotropy is a measure of polarization. Accordingly,

3. Claim 1 and 7 are rejected under 35 U.S.C. 102(e) as being anticipated by Wei et al. (US Patent 6,632,613).

Wei et al. discloses a fluorescence polarization (anisotropy) immunoassay for determining the presence or concentration of an analyte. Wei teaches contacting a fluorescent reference molecule (fluorescent labeled oligopeptide which binds a monoclonal antibody) and a fluorescent sensing molecule (monoclonal antibody which binds analyte) to radiation source to obtain a first level of anisotropy. Thereafter, Wei teaches exposing the aforementioned mixture to a sample containing unknown quantity of analyte which is capable of changing the intensity of fluorescence emitted by the

sensing molecule then obtaining a second level of anisotropy. Finally, Wei teaches correlating a change in the second level of anisotropy with the presence or concentration of analyte in the sample by comparing between the first and second anisotropy levels and control levels (see column 3, lines 49-63). The high-molecular weight analyte is a peptide, protein, or antibody (see Abstract and Examples). According to Wei, anisotropy is a parameter that is interrelated to fluorescence polarization and describes the same phenomena. However, anisotropy is used in the calculation of mole fraction or fluorescence fraction of bound tracers because it is additive with respect to these parameters and polarization is not. Wei teaches using anisotropy in calculating antigen-antibody binding constant since the denominator in the anisotropy definition is total fluorescent intensity (see column 6, line 59 to column 7, line 1).

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein

were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

4. Claims 2-6 and 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over by Wei et al. (US Patent 6,632,613) in view of Lakowicz et al. (US 5,660,991).

Wei has been discussed supra. Wei differs from the instant invention in failing to teach that the fluorescent reference molecule is a long-lifetime metal-ligand complex having an anisotropy near one or near zero, embedded in a stretched polymer film.

Lakowicz et al. disclose fluorescent reference molecules as long-lifetime metal-ligand complexes for coupling with proteins. The metal-ligand complexes display high anisotropy or polarization in the absence of rotational diffusion; thus are useful in immunochemical assays of high molecular weight analytes (see column 5, lines 42-63). The metal in the metal-ligand complex is ruthenium, osmium, or rhenium. The ligand in the complex can be pyridine 2 (bipyridine) or polypyridine (see column 8, lines 59-67). In practice, the metal-ligand complex is conjugated to a fluorescent sensing molecule (antibody, receptor, or lectin) which specifically binds an analyte, then exposed to radiation source (linearly polarized light) to cause light to be emitted from the mixture. Thereafter, the level of anisotropy is measured and compared to that from a control sample with known amount of analyte (see column 6. lines 46-60 and column 15, lines 31-36). The analyte detected is protein, antigen, nucleic acid, polysaccharide,

lipoprotein, glycoprotein, or foreign object (pharmacological agent) (see column 15, lines 37-44). Lakowicz et al. provide that asymmetric metal ligand complexes can display an anisotropy near zero or anisotropy near one, i.e. 0.25 to 0.3 (see column 18, lines 20-31). Additionally, Lakowicz et al. provide embedding the metal-ligand complexes in a stretched polymer film of 60% glycerol and 40% buffer, which forms an optically clear glass. In that environment, the metal-ligand complexes also display anisotropy values near zero or near one, i.e. 0.25 and 0.28, depending on the temperature (see column 18, lines 32-42).

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to substitute fluorescent metal-ligand complexes as taught by Lakowicz for the fluorescent reference molecules in the anisotropy method of Wei because metal-ligand complexes display long-lifetime and high anisotropy even in the absence of rotational diffusion and can be excited with simple light sources both of which are desirable for reducing auto-fluorescence. One of ordinary skill in the art at the time of the instant invention would have been motivated to incorporate metal-ligand complexes as taught by Lakowicz into the anisotropy method of Wei because metal-ligand complexes have a long luminescence lifetime which allows such probes to be used for immunochemical polarization or intensity assays of high molecular weight species.

### ***Double Patenting***

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11

F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

5. Claims 1-12 are rejected under the judicially created doctrine of double patenting over claims 1, 3, 4, 6-10, 12, and 13 of U. S. Patent No. 6,395,556 since the claims, if allowed, would improperly extend the "right to exclude" already granted in the patent.

The subject matter claimed in the instant application is fully disclosed in the patent and is covered by the patent since the patent and the application are claiming common subject matter, as follows: fluorescence polarization immunoassays which are based on polarization or anisotropy of emitted light when a sample is excited with vertically polarized light. Anisotropy is a measure of polarization, both anisotropy and polarization are said to describe the same phenomena.

Furthermore, there is no apparent reason why applicant was prevented from presenting claims corresponding to those of the instant application during prosecution of the application which matured into a patent. See *In re Schneller*, 397 F.2d 350, 158 USPQ 210 (CCPA 1968). See also MPEP § 804.

6. Claims 1-12 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 3, 4, 6-10, 12, and 13 of U.S. Patent No. 6,395,556 in view of Lakowicz et al. (US Patent 5,660,991).

US Patent 6,395,556 teaches anisotropy-based sensing method for measuring pH or concentration of labeled protein using fluorescent reference molecule which is fluorophore in stretch-oriented polymer film of polyvivnyl alcohol and pH sensitive fluorescein as fluorescence sensing molecule (6-carboxy fluorescein). The fluorescent reference molecule may be a metal-ligand complex. See column 1, line 36 to column 2, line 2. The metal ligand complexes are also known to be sensitive to oxygen and pH (see column 4, lines 23-38). According to US Patent 6,395,556, the fluorescent reference molecule may be a distinct entity but may have the same structure as the fluorescent sensing molecule, provided that the reference molecule is not exposed to the analyte, i.e. isolated in a separate compartment or the like. Alternatively, the fluorescent reference molecule can be embedded in a stretched polymer film so as not to be effected by the analyte (see column 4, lines 51-61). In practice, fluorescent reference molecules and fluorescent sensing molecules are provided and exposed to radiation; thus providing an initial reference position. Thereafter, the sensing molecule is exposed to analyte, then again, both are exposed to a radiation source to cause the molecules to emit combined fluorescence. The degree of rotation needed, relative to the initial reference position is correlated to the presence or concentration of analyte. See column 4, line 62 to column 5, line 30.

US Patent 6,395,556 differs from the instant invention in failing to specifically recite that the level of emission measured is that of anisotropy, rather than polarization.

Lakowicz et al. teach that fluorescence polarization or anisotropy immunoassays are based on the polarization or anisotropy of emitted light when a sample is excited with vertically polarized light. Lakowicz et al. specifically teach that polarization and anisotropy are interrelated and are said to describe the same phenomena.

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to incorporate the teaching of Lakowicz of anisotropy, into the fluorescence polarization method of US Patent 6,395,556 because both are interrelated so as to describe a same phenomena and since anisotropy is additive with respect to mole fractions or fluorescence fractions of bound tracers, its use is desirable in calculating antigen-antibody binding constants because the denominator in anisotropy definition is total fluorescent intensity.

7. No claims are allowed.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gailene R. Gabel whose telephone number is (571) 272-0820. The examiner can normally be reached on Monday, Tuesday, and Thursday, 5:30 AM to 2:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long V. Le can be reached on (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Gailene R. Gabel
Patent Examiner
Art Unit 1641
May 4, 2004

Christopher L. Chin

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